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TECH CENTER

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

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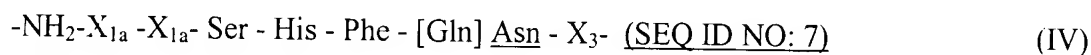
IN THE SPECIFICATION:

The paragraphs at page 20, line 12 to page 22, line 2 were amended as follows: TECH CENTER

In one embodiment the TGF- α polypeptide, related polypeptide, mimetic or functional fragment is a TGF- α polypeptide as set forth in SEQ ID NO:1, SEQ ID NO:3, or a TGF α mimetic selected from the group consisting of formula I, formula II, formula III, formula IV, or formula V, wherein formula I is:



wherein R_1 is $-NH_2$, or R_1 is R_3-X_3 , wherein R_3 is a polyethylene glycol (PEG) attached to the free NH_2 moiety of X_3 (wherein X_3 is Lys [or Arg] or Asp) and having a molecular weight of PEG of from about 2000 daltons to about 10,000 daltons, or one or more of the following seven amino acids from formula [VI] IV, including either L (natural) or D chiral orientations:



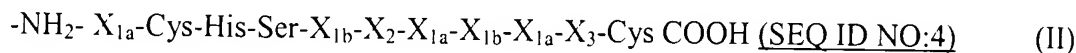
wherein $[X_1]$ X_{1a} is independently Val, Gly or Ala and X_3 is Lys [or Arg] or Asp;

wherein T is the native sequence of human TGF α (SEQ ID NO. 1) from amino acid residue no. 8 (Cys) to amino acid residue no. [44] 43 (Cys) consisting of native L amino acids; and wherein R_2 is $-COOH$ or one of more of the following seven amino acids, including either L (natural) or D chiral orientations, from formula V:



wherein X_4 is Glu or Asp, wherein X_5 is Leu or Ile, wherein X_6 is Asp or Glu, and wherein $[X_1]$ X_{1c} is independently Val, Gly, or Ala.

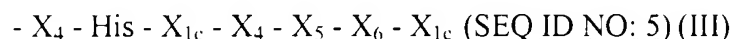
The invention provides a peptide having TGF- α biological activity, comprising at least an 11-membered peptide compound of formula II [(SEQ ID NO:4)]:



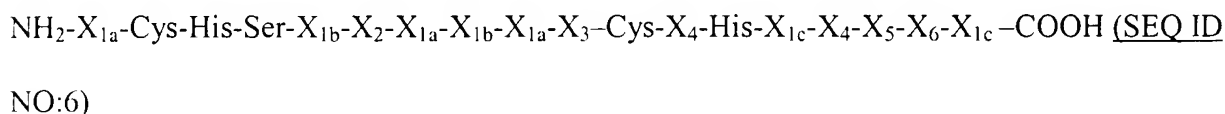
wherein $[X_1]$ is X_{1a} and X_{1b} are independently Val, Gly, or Ala, wherein X_2 is Tyr or Phe,

wherein X_3 is Arg or Lys, and wherein the two Cys moieties form a disulfide bond to create an 11-amino-acid functional peptide having a 10 member loop structure. In addition, at least one or

more of the following amino acids of formula III [(SEQ ID NO:5)] may be added to the C terminus Cys moiety of formula [I] II [(SEQ ID NO:4)]:

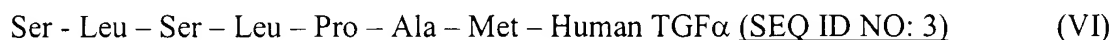


wherein X_4 is Glu or Asp, wherein X_5 is Leu or Ile, wherein X_6 is Asp or Glu and wherein X_{1c} is Val, Gly or Ala. Preferably, X_{1a} is Val, X_{1b} is Gly and X_{1c} is Ala thereby producing an 11, 12, 13, 14, 15, 16, 17 or 18 amino acid peptide. Preferably, X_2 is Tyr, and X_3 is Arg. Accordingly, in one embodiment the functional peptide of the invention has a sequence:



SEQ ID NO: 6 forms a 10 member loop structure with a 7 member tail that can be varied in length. In addition, SEQ ID NO: 6 can form dimmers comprising, for example, a 34-mer peptide. Accordingly, the functional peptide can be from about 10 to 18 amino acids in length (e.g. 10, 11, 12, 13, 14, 15, 16, 17, or 18 amino acids) wherein X_{1a} is Val, X_{1b} is Gly, X_{1c} is Ala and X_4 is [Gly] Glu and may also comprise hetero- or homo-dimers of various TGF- α peptides described herein. Such dimmers may have greater or reduced activities as compared to monomers.

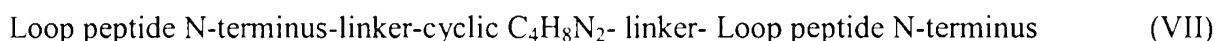
The invention further provides an active TGF- α 57 polypeptide (SEQ ID NO:3), wherein TGF- α 57 is a 57 amino acid polypeptide having the formula VI:



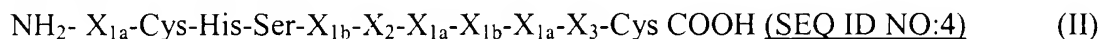
Wherein human TGF α is a 50 amino acid polypeptide having a sequence as set forth in SEQ ID NO:1.

The paragraphs at page 52, lines 1-27 were amended as follows:

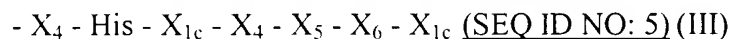
The invention further provides a bifunctional compound that acts as a TGF α mimetic, comprising a compound of formula III:



Wherein the linker moiety is designed to link the N-terminus of the Loop peptide to a nitrogen atom of the ring $C_4H_8N_2$ and wherein the "loop peptide" comprises at least an 11-membered peptide compound of formula II:



wherein X_{1a} and X_{1b} are independently Val, Gly, or Ala; X_2 is Tyr or Phe; X_3 is Arg or Lys; and the two Cys moieties are linked via a disulfide bond to form an at least 11-amino acid functional peptide having TGF- α activity. Preferably, at least one or more of the following amino acids are added to the C terminus Cys moiety from formula III, below:



wherein X_4 is Glu or Asp, wherein X_5 is Leu or Ile, [and] wherein X_6 is Asp or Glu and wherein X_{1c} is Val, Gly or Ala. Preferably, X_{1a} is Val, X_{1b} is Gly and X_{1c} is Ala. Preferably the linker group is independently selected from the group consisting of substituted or unsubstituted C_{1-6} alkoxy, xylenyl, wherein the substitutions are selected from the group consisting of: oxo, epoxy, hydroxyl, chloryl, bromyl, fluoryl, and amino. Preferably, X_2 is Tyr, and X_3 is Arg. Most preferably, the functional peptide is 18 amino acids in length wherein X_{1a} is Val, X_{1b} is Gly, X_{1c} is Ala and X_4 is [Gly] Glu.